9/13
C. Dossa
3/13/02

Dkt. 0575/62948/JPW/ADM

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Jingyue Ju et al.
U.S. Serial No.	:	09/823,181 Group Art Unit: 1655
Filed	:	March 30, 2001 Examiner: A. Chakrabarti
For	:	HIGH-FIDELITY DNA SEQUENCING USING SOLID PHASE CAPTURABLE DIDEOXYNUCLEOTIDES AND MASS SPECTROMETRY

1185 Avenue of the Americas
New York, New York 10036
February 11, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

AMENDMENT IN RESPONSE TO JANUARY 10, 2002 OFFICE ACTION

This Amendment is submitted in response to the Office Action issued January 10, 2002 by the U.S. Patent and Trademark Office in connection with the above-identified application. A response to the January 10, 2002 Office Action is due February 10, 2002. However, since February 10, 2002 is a Sunday, under 37 C.F.R. §1.7, a response may be filed on the next day which is not a Saturday, Sunday, or Federal Holiday, i.e. today, February 11, 2002. Accordingly, this Amendment is being timely filed.

Please amend the subject application as follows:

In the claims:

Please cancel claims 33-34, 36-37, 39, 41-43, 46, 48, and 50 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in a future continuation or

divisional application.

Please amend claims 4, 5, 7, 8, 11, and 15 as follows:

B1

4. (Amended) The method of claim 1 or 59, wherein the interaction between the chemical moiety attached via the linker to the DNA sequencing fragment and the compound on the surface comprises a biotin-streptavidin interaction, a phenylboronic acid-salicylhydroxamic acid interaction, or an antigen-antibody interaction.

5. (Amended) The method of claim 1 or 59, wherein the step of freeing the DNA sequencing fragment from the surface comprises disrupting the interaction between the chemical moiety attached via the linker to the DNA sequencing fragment and the compound on the surface.

B2

7. (Amended) The method of claim 1 or 59, wherein the dideoxynucleotide comprises a cytosine or a thymine with a 5-position, or an adenine or a guanine with a 7-position, and the linker is attached to the 5-position of cytosine or thymine or to the 7-position of adenine or guanine.

8. (Amended) The method of claim 1 or 59, wherein the step of freeing the DNA sequencing fragment from the surface comprises cleaving the linker.

B3

11. (Amended) The method of claim 1 or 59, wherein the linker comprises a derivative of 4-aminomethyl benzoic acid.

B4

15. (Amended) The method of claim 60 or 14, wherein a plurality of different linkers is used to increase mass separation between different labeled DNA sequencing

B4

fragments and thereby increase mass spectrometry resolution.

Please add new claims 59-73 as follows:

--59. (New) A method for sequencing DNA by detecting the identity of a plurality of dideoxynucleotides incorporated to the 3′ end of different DNA sequencing fragments using mass spectrometry, which comprises:

(a) attaching a chemical moiety via a linker to a plurality of different dideoxynucleotides to produce labeled dideoxynucleotides;

B5

(b) terminating a DNA sequencing reaction with the labeled dideoxynucleotides to generate labeled DNA sequencing fragments, wherein the DNA sequencing fragments have a 3′ end and the chemical moiety is attached via the linker to the 3′ end of the DNA sequencing fragments;

(c) capturing the labeled DNA sequencing fragments on a surface coated with a compound that specifically interacts with the chemical moiety attached via the linker to the DNA sequencing fragments, thereby capturing the DNA sequencing fragments;

(d) washing the surface to remove any non-bound component;

(e) freeing the DNA sequencing fragments from the surface; and

(f) analyzing the DNA sequencing fragments using mass spectrometry so as to sequence the DNA.--

--60. (New) The method of claim 59, wherein the chemical moiety is attached via a different linker to different dideoxynucleotides.--

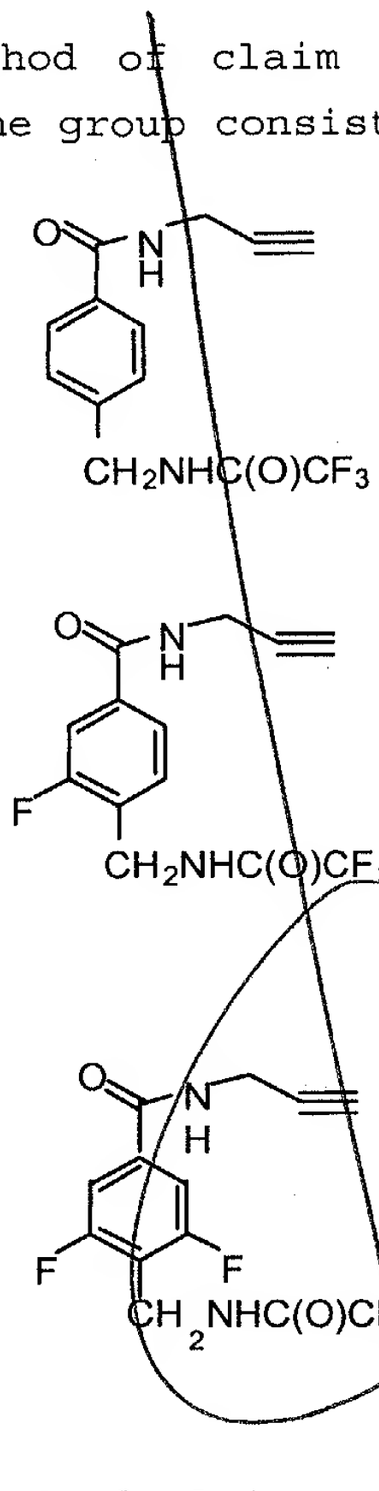
--61. (New) The method of claim 5, wherein the interaction is disrupted by a means selected from the group consisting of one or more of a physical means, a chemical means, a physical chemical means, heat, and light.--

B5

--62. (New) The method of claim 8, where the linker is cleaved by a means selected from the group consisting of one or more of a physical means, a chemical means, a physical chemical means, heat, and light.--

--63. (New) The method of claim 62, wherein the linker is cleaved by ultraviolet light.--

--64. (New) The method of claim 12, wherein the linker is selected from the group consisting of:



,

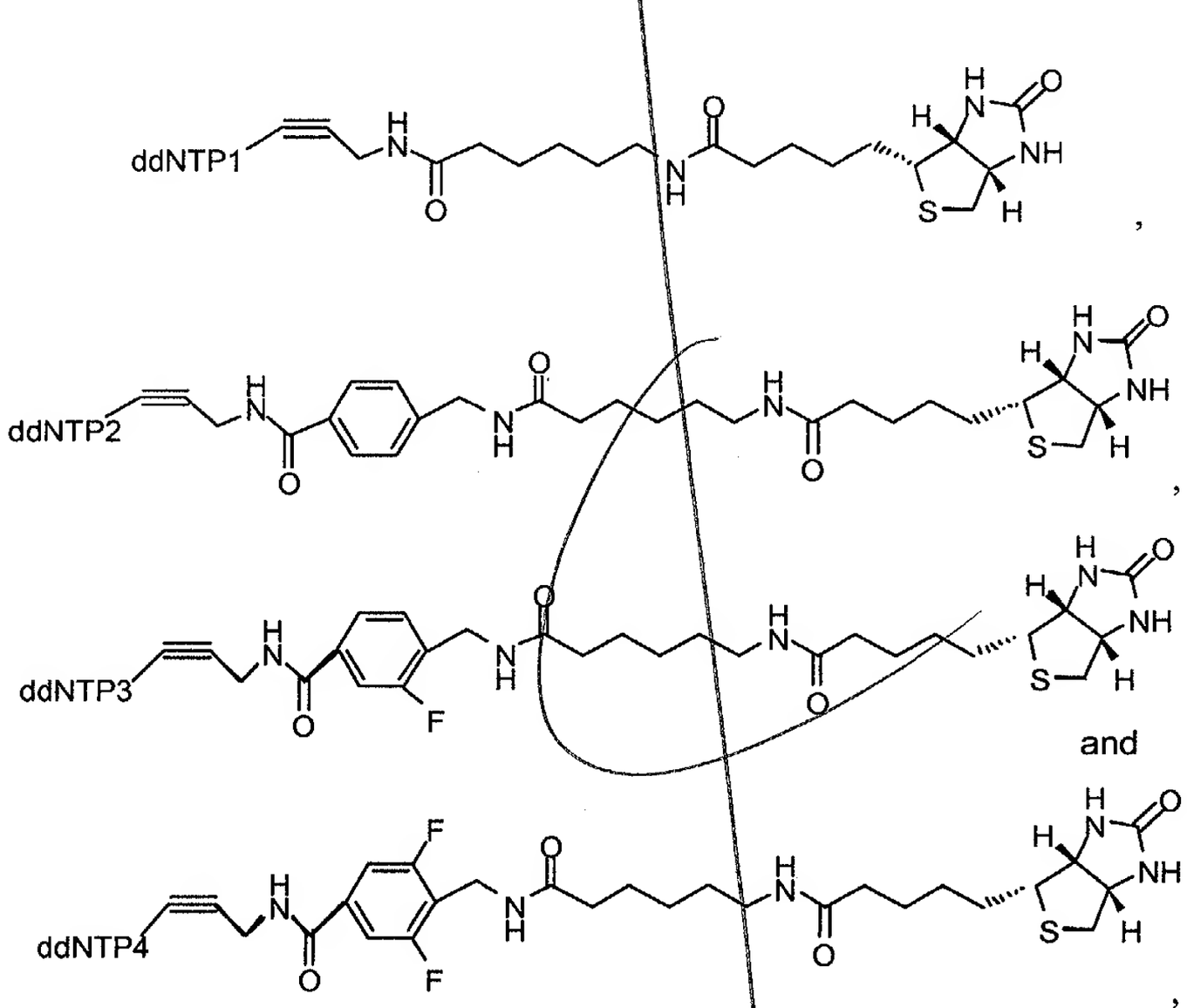
and

.--

--65. (New) The method of claim 1 or 59, wherein the chemical moiety comprises biotin, the labeled dideoxynucleotide is a biotinylated dideoxynucleotide, the labeled DNA sequencing fragment is a biotinylated DNA sequencing fragment, and the surface is a streptavidin-coated solid surface.--

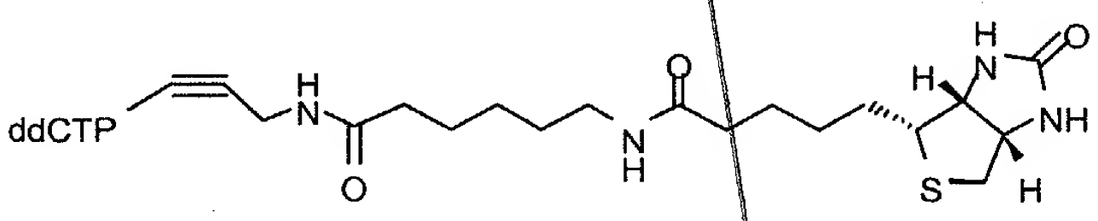
--66. (New) The method of claim 65, wherein the biotinylated dideoxynucleotide is selected from the group consisting of ddATP-11-biotin, ddCTP-11-biotin, ddGTP-11-biotin, and ddTTP-16-biotin.--

--67. (New) The method of claim 65, wherein the biotinylated dideoxynucleotide is selected from the group consisting of:

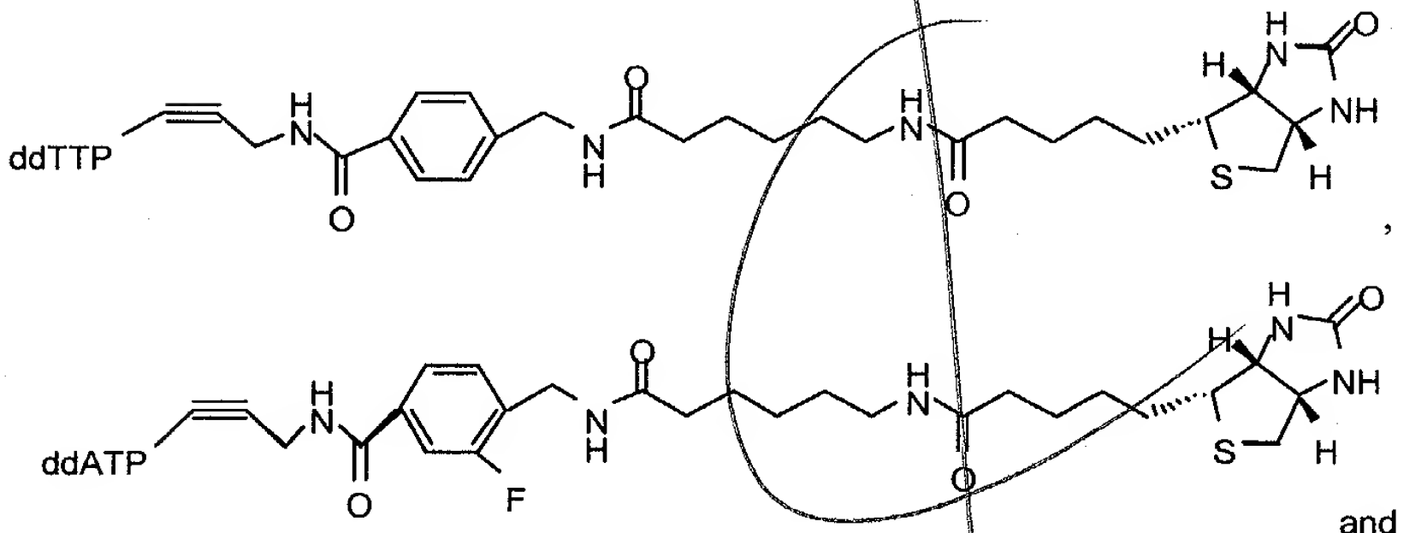


wherein ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides.--

--68. (New) The method of claim 67, wherein the biotinylated dideoxynucleotide is selected from the group consisting of:

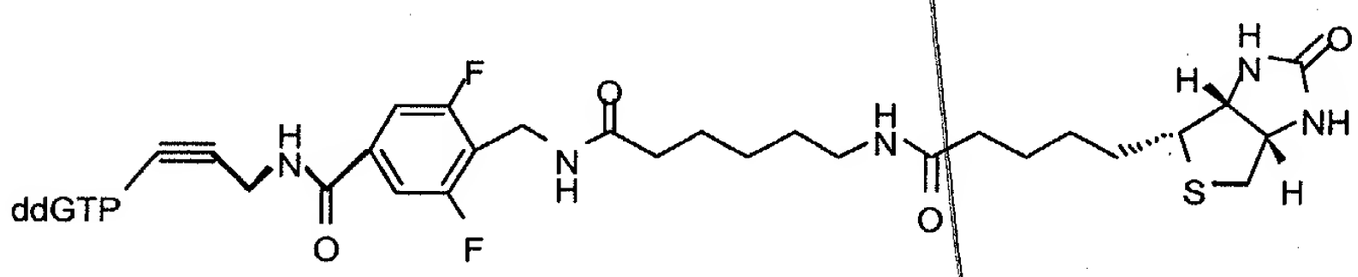


,



,

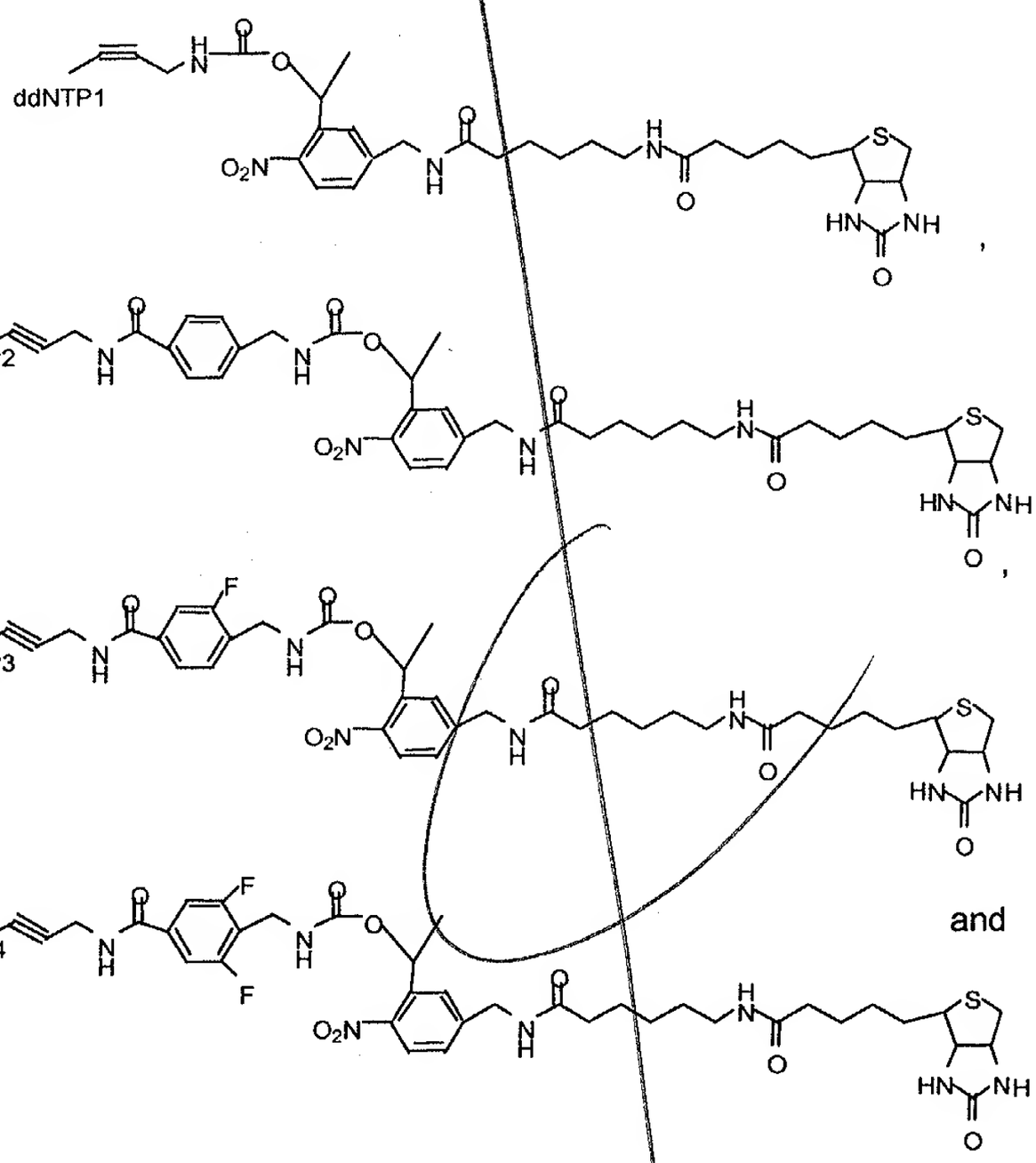
and



.

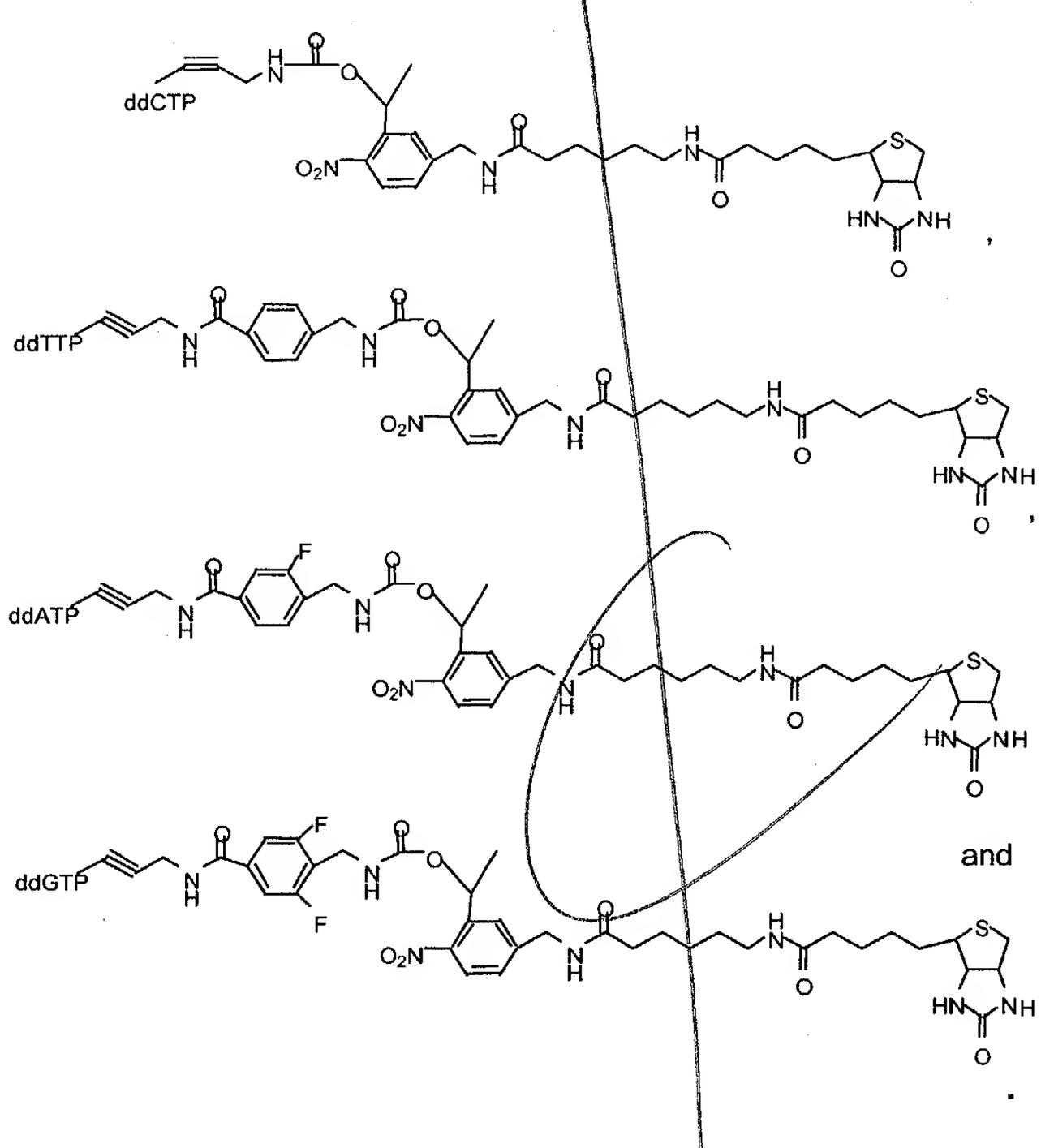
--

--69. (New) The method of claim 65, wherein the biotinylated dideoxynucleotide is selected from the group consisting of:



wherein ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides.--

--70. (New) The method of claim 69, wherein the biotinylated dideoxynucleotide is selected from the group consisting of:



--

--71. (New) The method of claim 65, wherein the streptavidin-coated solid surface is a streptavidin-coated magnetic bead or a streptavidin-coated silica glass.--

--72. (New) The method of claim 1 or 59, wherein steps (b) to (e) are performed in a single container or in a plurality

of connected containers.--

--73. (New) Use of the method of claim 1 or 59 for detection of single nucleotide polymorphisms, genetic mutation analysis, serial analysis of gene expression, gene expression analysis, identification in forensics, genetic disease association studies, genomic sequencing, translational analysis, or transcriptional analysis.--

A marked-up version of the amended claims showing the changes made is attached hereto as **Exhibit 1**.

REMARKS

Claims 1, 4-5, 7-8, 11-12, 14-15, 33-34, 36-37, 39, 41-43, 46, 48, and 50 were pending in the subject application. By this Amendment applicants have canceled claims 33-34, 36-37, 39, 41-43, 46, 48, and 50 without prejudice or disclaimer; amended claims 4, 5, 7, 8, 11, and 15; and added new claims 59-73. Accordingly, upon entry of this Amendment claims 1, 4-5, 7-8, 11-12, and 14-15 as amended and new claims 59-73 will be pending and under examination.

Applicants maintain that the amendments to claims 4, 5, 7, 8, 11 and 15, and the addition of new claims 59-73 raise no issue of new matter and are fully supported by the specification as filed. Claims 4, 5, 7, 8, 11 and 15 were amended to change claim dependency. Support for new claim 59 may be found inter alia in the specification, as originally-filed, on page 16, lines 5-32. Support for new claim 60 may be found inter alia in the specification, as originally-filed, on page 17, lines 1-3. Support for new claim 61 may be found inter alia in the specification, as originally-filed, on page 17, lines 27-31. Support for new claims 62 and 63 may be found inter alia in the specification, as originally-filed, on page 18, lines 14-19. Support for new claim 64 may be found inter alia in the specification, as originally-filed, on page 18, line 27 through page 19, line 9. Support for new claims 65 and 66 may be found inter alia in the specification, as originally-filed, on page 19, lines 18-26. Support for new claim 67 may be found inter alia in the specification, as originally-filed, on page 20, lines 1-10. Support for new claim 68 may be found inter alia in the specification, as originally-filed, on page 21, lines 1-5. Support for new claim 69 may be found inter alia in the specification, as originally-filed, on page 22, lines 1-10. Support for new claims 70-72 may be found inter alia in the specification, as originally-filed, on page 23, lines 1-11. Support for new claim 73 may be found inter alia in the specification, as originally-filed, on page 24, lines 4-10.

Accordingly, applicants respectfully request that this Amendment be entered.

Restriction Requirement Under 35 U.S.C. §121

In the January 10, 2002 Office Action, the Examiner to whom the

subject application is assigned stated that restriction to one of the following inventions is required under 35 U.S.C. §121:

I. Claims 1, 4-5, 7-8, 11-12, 14-15, and 41, drawn to method of hybridization of nucleic acids;

II. Claims 33-34, 36-37, and 39, drawn to nucleic acids; and

III. Claims 42-43, 46-48, and 50, drawn to a purification device.

In support of the restriction requirement, the Examiner alleged that the inventions are distinct, each from the other because of the following reasons. The Examiner alleged that the inventions of Group I and II are related as product and process of use. The Examiner stated that inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the Examiner stated that the nucleic acids of Group II can be used in the method of nucleic acid hybridization of Group I or can be used to make RNA and protein and can be used to make antisense nucleic acids for gene therapy.

The Examiner alleged that the inventions of Groups I and III are unrelated. The Examiner stated that inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the Examiner stated that the different inventions of method of nucleic acids hybridization of Group I are not disclosed as capable of use together with the purification device of Group III and they have different modes of operation, different functions, or different effects.

The Examiner stated that the inventions of Groups II and III are unrelated. The Examiner stated inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP §808.01). In the instant case, the Examiner stated that the different inventions of nucleic acids of Group II are not disclosed as capable of use together with the purification device of Group III and they have different modes of operation, different functions, or different effects.

The Examiner concluded that because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The Examiner advised applicants that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 C.F.R. §1.143).

In response to this restriction requirement, applicants hereby elect, with traverse, to prosecute the invention of Group I, which the Examiner characterized as drawn to methods of hybridization of nucleic acids. Applicants maintain that new claims 59-73 are drawn to the method identified by the Examiner as Group I.

Applicants note that 35 U.S.C. §121 states, in part, that "[i]f two or more independent and distinct inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions." [Emphasis added].

Applicants request that the restriction requirement be withdrawn in view of the fact that the claims of the Groups I, II, and III are not independent.

Under M.P.E.P. §802.01, "independent" means "there is no disclosed relationship between the ... subjects disclosed, that is, they are unconnected in design, operation, or effect... ." The claims of Groups I, II, and II are related in that they are drawn to methods for sequencing DNA and to labeled dideoxynucleotides and separation systems which can be used in those methods.

Applicants therefore respectfully assert that two or more independent and distinct inventions have not been claimed in the subject application because the groups are not independent under M.P.E.P. §802.01.

Additionally, applicants point out that under M.P.E.P. §803, the Examiner must examine the application on the merits, even though it includes claims to distinct inventions, if the search and examination of an application can be made without serious burden. There are two criteria for a proper requirement for restriction, namely (1) the inventions must be independent and distinct; AND (2) there must be a serious burden on the Examiner if restriction is not required.

Applicants maintain that there would not be a serious burden on the Examiner if restriction were not required. A search of prior art with regard to Groups I-III would necessarily identify art for other Groups. Since there is no serious burden on the Examiner to examine Groups I-III in the subject application, the Examiner must examine the entire application on the merits.

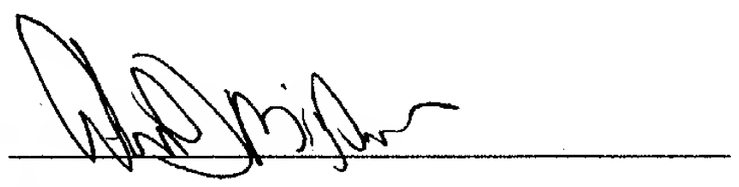
Accordingly, in view of the preceding remarks, applicants

respectfully request that the Examiner reconsider and withdraw the requirement for restriction.

If a telephone conference would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

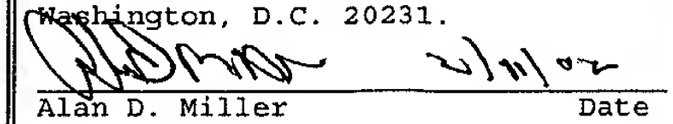
No fee, other than the enclosed $356.00 filing fee, is deemed necessary in connection with the filing of this Amendment. However, if an additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Registration No. 28,678
Alan D. Miller
Registration No. 42,889
Attorneys for Applicants
Cooper & Dunham LLP
1185 Ave of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Assistant Commissioner for Patents, Washington, D.C. 20231.



Alan D. Miller Date
Reg. No. 42,889